PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4018PTWO/er	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/EP2004/051209	International filing date *(day/month/year)* 23.06.2004	Priority date *(day/month/year)* 25.06.2003
International Patent Classification (IPC) or national classification and IPC A61K31/715, A61P17/02		
Applicant BIOPLAX LIMITED		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
25.04.2005	08.09.2005
Name and mailing address of the International preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Bonzano, C Telephone No. +31 70 340-2202

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/051209

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-8 as originally filed

   Claims, Numbers

   1-6 received on 25.04.2005 with letter of 25.04.2005

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/051209

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	1-6
	No:	Claims	-
Industrial applicability (IA)	Yes:	Claims	1-6
	No:	Claims	-

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V.

1. The following documents are referred to in this communication:

D1 : US 5 972 906 A (FALK RUDOLF EDGAR ET AL) 26 October 1999 (1999-10-26)

D2 : US 2002/183278 A1 (BRAGUTI GIANLUCA ET AL) 5 December 2002 (2002-12-05)

D3 : RUSSELL A L: "PARALLELISM BETWEEN CUTANEOUS AND MUCOSAL PATHOLOGY. A NEW TEST BEDFOR AT 2101 (3% DICLOFENAC ACID IN 2.5% HYALURONAN)" ROYAL SOCIETY OF CHEMISTRY. ROUND TABLE SERIES, ROYAL SOCIETY OF MEDICINE SERVICES, LONDON, GB, vol. 40, 1 December 1995 (1995-12-01), pages 125-131, XP000603132 ISSN: 0268-3091

Novelty

2.1 The present application meets the criteria of Article 33(1) PCT, because the subject-matter of claims 1-6 is new in the sense of Article 33(2) PCT.

Document D1 discloses the use of topical hyaluronic acid or sodium hyaluronate together with NSAIDs, for treating aphthous and other oral ulcerations, and burning mouth syndrome. Example of formulations is 2.5% by weight of hyaluronic acid, which is within the limit of claim 4. The average molecular weight is less than 750000 daltons. Document D3 discloses that subjects with aphthous mouth ulcers where treated with a compositions consisting of hyaluronan and diclofenac. Hyaluronan has a role as healing agent. Hyaluronan is a synonim for hyaluronic acid.

The subject-matter of claims 1-6 is therefore new, because different percentages are claimed and hyaluronic acid is never administered as a sole ingredient. (Article 33(2) PCT).

2.2 Document D2 discloses compositions containing as active ingredients polyvinylpirrolidone and hyaluronic acid having average molecular weight of 1.6-2.2 million daltons for treating mucositis, stomatitis, aphthous ulcerations. The average molecular weight is included in the limit claimed in claim 1. However hyaluronic acid is not the sole active ingredient.

The subject-matter of claims 1-6 is therefore new over D2 (Article 33(2) PCT).

Inventive step

3.1 The present application doesmeet the requirements of Article 33(3) PCT, because the subject-matter of claims 1-6 involves an inventive step over D1.

5.2 Document D2 discloses compositions containing as active ingredients polyvinylpirrolidone

and hyaluronic acid having average molecular weight of 1.6-2.2 million daltons for treating mucositis, stomatitis, aphthous ulcerations. The average molecular weight is included in the limit claimed in claim 1. However hyaluronic acid is not the sole active ingredient.
The present application differs in that the same disease is treated in the same patients using hyaluronic acid alone.
The problem to be solved by the present invention may therefore be regarded as finding an alternative treatment to oral cavity aphthas.
Therefore, being aware that hyaluronic acid has an activity against the claimed disorder together with PVP, the person skilled in the art would not have been inevitably led to use the hyaluronic acid alone for treating the claimed disorders. The skilled person would not have expected for the hyaluronic acid alone the same effect described in document D2, as D2 discloses that the favorable therapeutic results obtained by the use of the compositions of hyaluronic acid with PVP are believed to be due to the interactions between hyaluronic acid, or a pharmaceutically acceptable salt thereof, and polyvinylpyrrolidone.

NEW SET OF CLAIMS

1. Use of hyaluronic acid for preparing compositions for the treatment of oral cavity aphthas, wherein hyaluronic acid is the sole active ingredient and the average molecular weight of hyaluronic acid is comprised between 800,000 and 4,000,000.

2. Use as claimed in claim 1 wherein the hyaluronic acid is in the form of sodium salt.

3. Use as claimed in claim 2 wherein said compositions are suitable for topical application.

4. Use as claimed in claim 3 wherein said compositions for topical use contain sodium hyaluronate in concentrations between 0.01 and 10% by weight on the total weight of the composition.

5. Use as claimed in claim 4, characterised in that said concentration is between 0.01 and 5% by weight on the total weight of the composition.

6. Use as claimed in any one of claims 1-5, wherein said average molecular weight of the hyaluronic acid is between 1,000,000 and 2,000,000.